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ARCHIVES OF PEDIATRICS

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DISEASES OF INFANTS AND CHILDREN
JOHN FITCH LANDON, M.D., Editor

LEADING ARTICLES IN THIS NUMBER

Hemoglobins: Nomenclature and Abnormal Hemoglobins and Their Relationship to Hemolytic Disease. Review of Literature.
William J. Holoday, M.D. 39

The Developmental Mechanics of Heart Malformations.
Hans Mautner, M.D. 47

Pediatrics at the Turn of the Century.
Causative Factors of the Paralyses of Early Life.
Royal Storrs Haynes, M.D. 65

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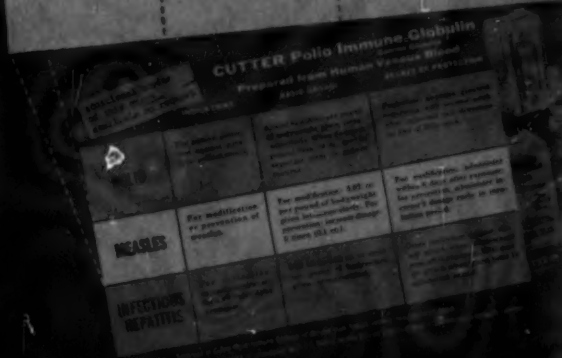

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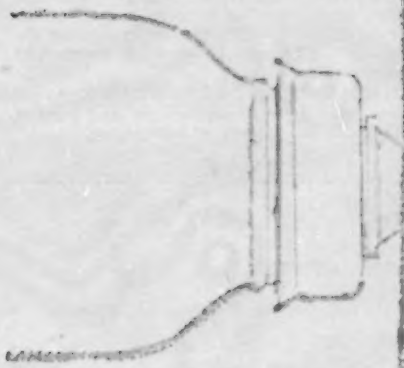

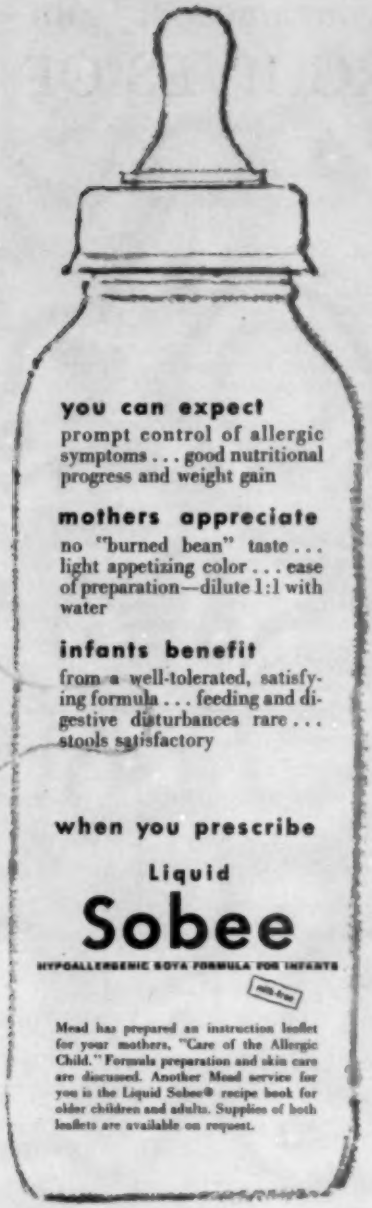

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CONTENTS

ORIGINAL COMMUNICATIONS

Hemoglobins: Nomenclature and Abnormal Hemoglobins and Their Relationship to Hemolytic Disease. Review of Literature.
WILLIAM J. HOLADAY, M.D. 39

The Developmental Mechanics of Heart Malformations.
HANS MAUTNER, M.D. 47

PEDIATRICS AT THE TURN OF THE CENTURY

Causative Factors of the Paralyses of Early Life.
ROYAL STORRS HAYNES, M.D. 65

DEPARTMENT OF ABSTRACTS

Money, J.; Hampson, J. G. and Hampson, J. L.: Hermaphroditism: Recommendations Concerning Assignment of Sex, Change of Sex and Psychologic Management 72

Craig, J. O.: Oral Factors in Accidental Poisoning 73

(Continued on page 4)

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(Continued from page 2)

Bodian, D.; Francis, T. Jr.; Larson, C.; Salk, J. E.; Shope, R. E.; Smadel, J. E. and Shannon, J. A.: Interim Report, Public Health Service Technical Committee on Poliomyelitis Vaccine 73

Lawrence, R. and Carmichael, D. B.: Myocarditis in Acute Poliomyelitis.... 73

Roberts, M. H. and Sullivan, C.: Influence of the Liver on Bone Metabolism. Report of Two Cases..... 74

Clark, D. E.: Association of Irradiation with Cancer of the Thyroid in Children and Adolescents..... 74

Handy, V. H. and Goldberg, I. D.: The Occurrence of Malignancies in Children 75

BOOK REVIEWS

Psychopathology and Education of the Brain-Injured Child. By Alfred A. Strauss and Newell C. Kephart..... 76

Communicable Diseases. 3rd Ed. By Franklin H. Top, M.D. and Collaborators 76

ITEMS

Cardiospasm in Children..... 46

Rupture of the Liver in a Newborn Infant with Recovery..... 64

Smallpox Vaccination with Subsequent Occurrence of Poliomyelitis..... 71

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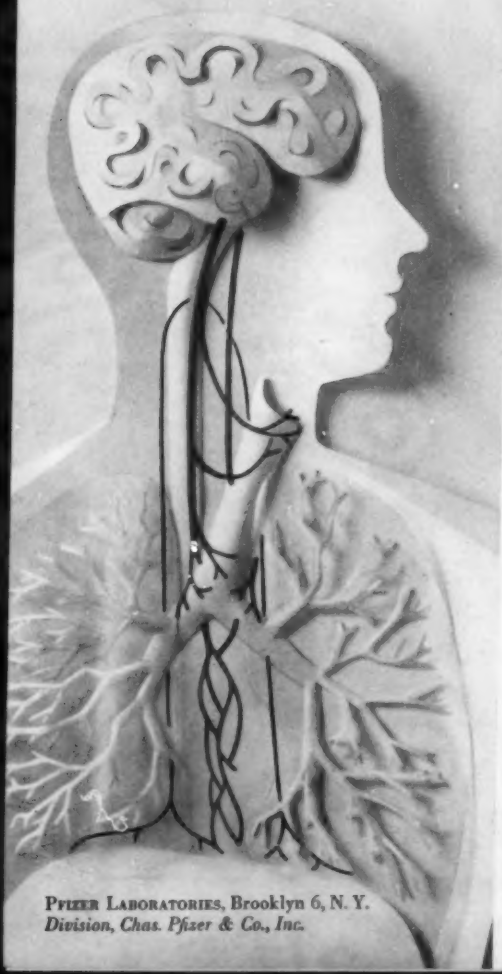

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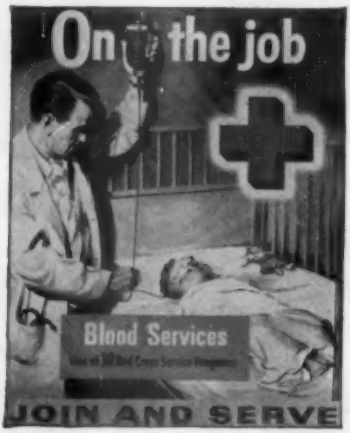

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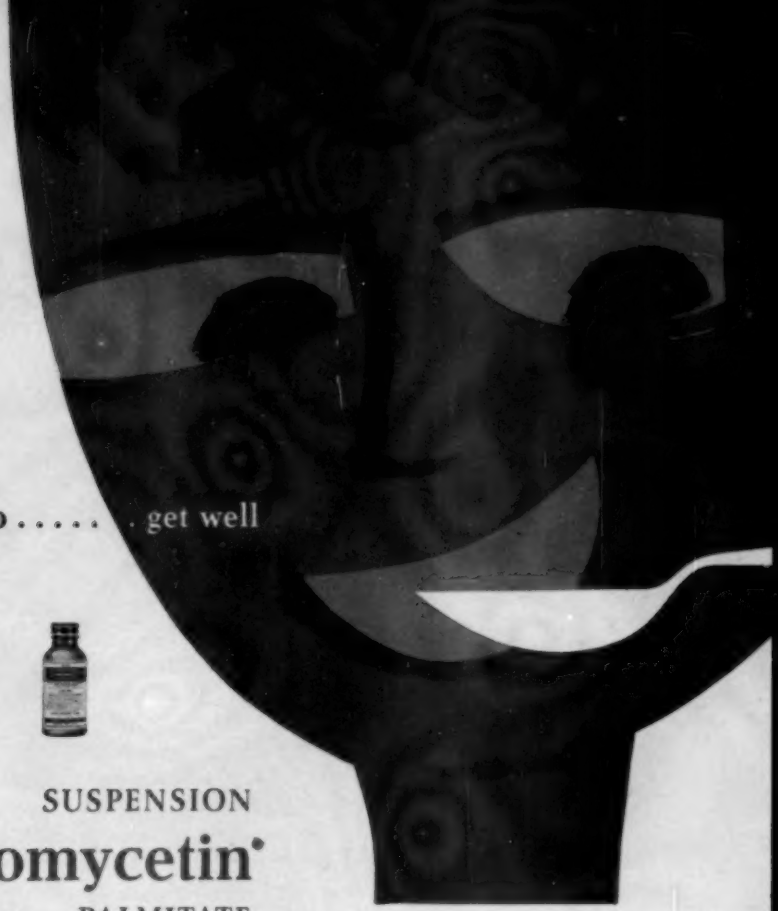

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1. Manheim, S. D., et al: "Further Observations on Anorectal Complications Following Aureomycin, Terramycin and Chloromycetin Therapy." N. Y. State Jrnl. Med., 54:37-1, Jan., 1954.
2. Curry, J. C. and Barber, F. W.: Bacteriological Proceedings, 1951, of The Society of Am. Bact., page 23.
3. Grossman, L., St. Francis Hospital, Miami Beach, Fla., to be published.
4. Niedelman, M. L., et al: Jrnl. Ped., 37:762, Nov., 1950.
5. Bleier, A. H., et al: Arch. Ped., 69:445, Nov., 1952.
6. Benson, R. A., et al: Jrnl. Ped., 31:369, Oct., 1947.
7. Ibid: Jrnl. Ped., 34:49, Jan., 1949.

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HEMOGLOBINS: NOMENCLATURE AND ABNORMAL HEMOGLOBINS AND THEIR RELATIONSHIP TO HEMOLYTIC DISEASE.

Review of Literature.

William J. Holaday, M.D.
Eau Claire, Wis.

Hemoglobin, the coloring pigment of the blood and the main oxygen carrying component of the blood, has become the object of intensive laboratory research. The problem was suggested by the biological experiment of sickle cell anemia, the presence of this disease suggesting a difference in the red cell from normal. When it was determined that these same cells sickled in an atmosphere of reduced oxygen tension, it then became evident this abnormality of the cell was contained within the oxygen carrying component of that cell, namely the hemoglobin. The problem then is the nature of the abnormality.

Hemoglobin, being composed of *heme*, the iron containing pigment, specifically an iron porphyrin, and *globin*, a protein of the histone class, forms a loose combination with oxygen, the iron being in the ferrous state. Porphyrins are pigments which form the basis of the more complex compound heme. The basic nucleus upon which all porphyrins are built consists of four pyrrol rings. (Fig. 1.)

These four pyrrol rings, when linked together by methene couplings into a larger ring-like structure, form the parent structure porphin. (Fig. 2.).

By the addition of ethyl, methyl, vinyl or propionyl groups the body syntheses so-called porphyrin Type III or protoporphyrin.[2]

Porphyrins are capable of forming compounds with various metals, in the instance of protoporphyrin combined with the Fe atom the compound heme is formed. The atom of iron in the ferrous state is believed to be attached to the porphyrin as represented in[2] Figs. 4 and 5.

Heme is capable of combining with various proteins; when combined with the protein globin, the compound hemoglobin is produced.

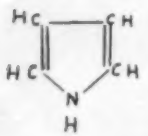

Fig. 1. Pyrrol.

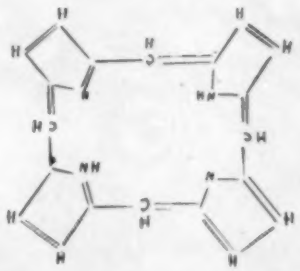

Fig. 2. Porphin.

Electrophoresis, namely the movement of a charged particle in an external electrical field, has been utilized as a method of studying hemoglobins. The apparatus and technique were first adequately described by Tiselius of Sweden.[3] Simply stated, the method considers the patterns of movement of particles in an electrical field adequately buffered and of proper pH. The particles, depending upon their charge and molecular weight, move at a certain speed, distance and direction in a standardized apparatus. The particles of similar charge and molecular weight gather at a particular point in the electrical field. The group of proteins may be photographed, or projected through an optical system upon a screen; or, they may be allowed to move through the electrical field upon a sensitized filter paper, thus, so to speak, photographing their own movements. The net result is that a specifically charged particle constantly forms a particular pattern in respect to the standardized field. Thus a particle may be identified because of its pattern, and, just as important, may be differentiated from related compounds because of its electrical charge.[4, 5, 6]

Nomenclature. Research workers, in the United States and

abroad, have been intensifying their attack upon the identification of different types of human hemoglobin. As a result, several nomenclatures have been devised. Singer, Chernoff and Singer, in 1951, writing at a time when only normal, fetal and sickle cell hemoglobins were recognized, proposed the nomenclature: N=normal adult, F=normal fetal, and S=sickle cell hemoglobin. Later,

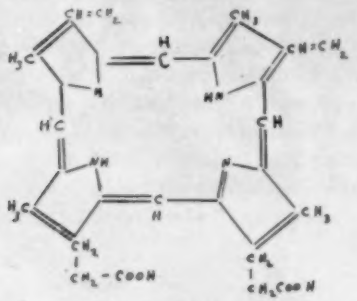

Fig. 3. Porphyrin—Type III.

Kaplan, Zuelzer and Neel suggested that since the field was in a state of flux, that the hemoglobins be numbered in the order of their identification. They proposed 1=normal adult, 2=sickle cell, 3=a new hemoglobin they described in 1951, now designated as hemoglobin 'c'. However, as work progressed, it became evident that the existing nomenclatures were inadequate as they stood. It was found that normal adult and normal fetal were found together, also it was found that in the sickle cell trait there was a mixture of normal and sickle cell hemoglobin. Thus, in 1951, Itano described the following nomenclature, which has since been accepted by Neel and his co-workers in Chicago.

	Name		Letter
Itano Nomenclature:[9]	Normal adult	(N)	'a'
	Normal fetal	(F)	'f'
	Sickle cell	(S)	'b'
	.....	(3)	'c'
	.....		'd'

Types of Hemoglobin: The possibility that there might exist more than one form of hemoglobin in the human was suggested by the work of Von Korber in the late 1800's.[10] This worker noticed there was a difference in the time needed for the denaturation of fetal hemoglobin as compared with adult hemoglobin. This work has been corroborated by the use of the spectroscope.

More recent work concerning fetal hemoglobin[11] and its relationship to the alkali-resistant-factor has been done by Singer and Chernoff.[7, 12] These studies, plus other work, have substantiated 'f' hemoglobin to be the normal hemoglobin of the fetus, 'f' hemoglobin has a U-V[13] spectrum and molecular weight similar to that of 'a' normal adult hemoglobin. The two differ in their resistance to alkali denaturization,[12] immunologic properties,[14] electrophoretic pattern,[15] and mobility.[16] Recent work has suggested that the reason fetal erythrocytes resist sickling is because of the presence of 'f' hemoglobin,[18] which does not sickle. The red cells

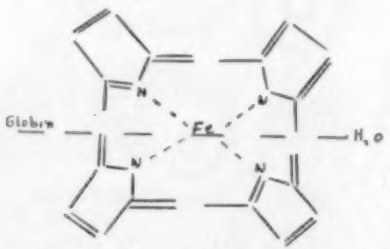

Fig. 4. Reduced Hemoglobin.

of a twenty-week fetus were found to contain 94 per cent 'f' hemoglobin, while the cells of a four-month infant were found to contain 10-20 per cent 'f' hemoglobin. Thus the decrease in 'f' hemoglobin with the concomitant increase in 'b' hemoglobin in those infants inheriting 'b' hemoglobin is believed to account for the delay in the appearance of sickle cell anemia in infants. Recent work by Singer and Chernoff[7] suggest there may be prolonged production of 'f' hemoglobin in infants with hemolytic disease, and reactivation of its production in certain adult blood dyscrasias.

Pauling and associates[19] have demonstrated that 'a' and 'b' hemoglobins move as oppositely charged ions in appropriately charged electrical fields. Studies by workers, including Itano,[16] have shown

'b' hemoglobin differs from 'a' hemoglobin in respect to its isoelectric point, and its mobility at different pH's. Singer, Chernoff and associates[12] have suggested that of the known hemoglobins to date only 'b' hemoglobin is capable of forming gels or tactoids. Perutz and Mitchison,[20] in 1950, found the reduced form of 'b' hemoglobin to be crystalline, differing in this respect from 'a' hemoglobin; these workers suggested a molecular difference as the etiology. Pauling and others[19] found no significant difference in the acidic and basic amino acid contest of 'a' and 'b' hemoglobins;[20] however, it was felt there was a probable difference in the relationship of certain amino acids in their composition.[21] This difference in the physical relationships of the amino acids is believed to effect the folding of the molecule in respect to differing oxygen tensions. Thus the work suggests a molecular difference in 'b' hemoglobin[21] as compared with normal hemoglobin. This

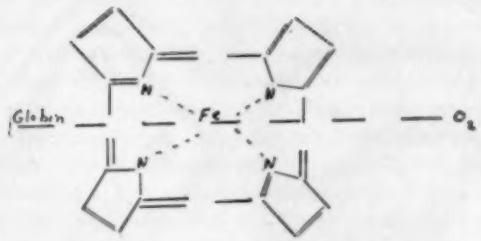

Fig. 5. Oxygenated Hemoglobin.

molecular difference is reflected in the abnormal physical properties not displayed by 'a' or normal adult hemoglobin. The "abnormal" physical response of 'b' hemoglobin is of clinical value when one considers the sickling phenomena under reduced oxygen tensions. Pauling and associates,[19] in 1949, felt that since the sickling occurs only under reduced oxygen pressure, the molecular difference between hemoglobin 'a' and 'b' is closely related to the oxygen carrying ion of the molecule, i.e., the Fe ion.

Neel and his associates, in December 1951, described for the first time hemoglobin[8] 'c'. Since this was the third hemoglobin to be identified by electrophoretic means ('f' is not identified by this method), it was originally designated hemoglobin '3'.

At the time of Neel's original paper, no case of homozygous hemoglobin 'c' disease had been located, and the original work was done on patients with combinations of 'a' and 'c', as well as 'b' and 'c'. Comparison of these patients with those with sickle cell anemia and sickle cell trait led to several points of differential other than electrophoretic pattern. Hereditary studies were used as a check on the laboratory methods.

Ranny, Larson and McCormack,[23] in 1953, described a case of homozygous hemoglobin 'c' disease; they described the clinical and laboratory aspects of the homozygous form as compared to the mixtures as described by themselves and Neel. These clinical and laboratory pictures are presented below:

Homozygous 'c': a. no symptoms, b. spleenomegoly of long duration, c. hemoglobin of 10-12 grams, d. mild reticulocytosis, e. nearly all the RBC are target cells, f. no crisis such as in sickle cell anemia.

Heterozygous Hemoglobin 'b' and 'c' Disease: a. milder than sickle cell anemia, b. hemoglobin of approximately 10 grams, c. progressive splenic enlargement, d. history of arthritic pain, e. questionable bone changes, f. mild reticulocytosis, g. target cells of 50-60 per cent; Neel, and associates, found essentially the same picture with the additions of h. increased resistance of cells to hypotonic saline, i. mild hemolytic phenomena, j. decreased survival time with a half life of 12 days, k. sickling in vitro with decreased oxygen pressures.

Heterozygous Hemoglobin 'a' and 'c' Disease: a. symptom free, b. hemoglobin of 11 to 12 grams, c. normal reticulocyte count, d. very few target cells; Neel in the original paper on this disease noted e. optimal RBC and hemoglobin values, f. no evidence of hemolytic processes, g. target cells, well beyond the normal range of 3-5 per cent, h. decreased survival time with a half life of 18 days.

Hemoglobin 'c' alone and in combination with others, as described above, may be suspected with relatively simple laboratory and clinical means; however, absolute identification is established by identifying the physical properties of the hemoglobin in question.

Itano, in December 1951,[9] described another abnormal hemoglobin, hemoglobin 'd'. The above investigator, while studying

the hemoglobins of a particular family, noted some members had erthrocytes which sickled and contained hemoglobin physically similar to hemoglobin 'b'. He also noted that the father was a typical carrier of the sickle cell trait. However, in other members of the family, he found hemoglobin which behaved electrophoretically similar to hemoglobin 'b', but which did not sickle. He found this hemoglobin present in the cells of the mother, and postulated she was the carrier of the trait. In an effort to differentiate between these two hemoglobins with similar electrophoretic patterns, Itano investigated their relative solubilities. He found hemoglobin 'd' to have a solubility similar to 'a', which is five to seven times the solubility of hemoglobin 'b'. The exact place hemoglobin 'd' is to take in the etiology of hemolytic disease is yet to be determined.

Thus, in summation, the abnormal and fetal hemoglobins have been described in relationship to the normal adult hemoglobin and to themselves. The methods of investigation have been mentioned in part as well as some of the results. Several clinical pictures have been suggested together with some of their differential points. An attempt has been made to mention the existing nomenclatures and their relationship, in the hope that the casual reader may keep abreast of the ever growing literature. As with all reviews, it suffers from lack of detail and inaccuracies. However, since its main function was to clarify the nomenclature, which in itself makes the literature incomprehensible, wtihout extensive review, there is hope some sort of rough path has been opened to a growing field of investigation.

REFERENCES

1. Kleiner: Human Biochemistry, 3rd Ed., p. 170.
2. Best and Taylor: Physiological Basis of Medical Practice, 5th Ed., pp. 52-54.
3. Electrophoretic Analysis and Constituents of Native Fluids. Harvey Lectures, 35: 37, 1940.
4. Kleiner: Human Biochemistry, 3rd Ed., p. 109.
5. Eelctrophoresis in Medicine. Yale J. Biol. & Med., 19: 67, 1946.
6. Electrophoresis. Ann. New York Acad. Sc., 39: 105, 1939.
7. Singer; Chernoff and Singer: Studies on Abnormal Hemoglobins. Blood, 6: 413, 1951.
8. Kaplin; Zuezeth; Eugene; Wolf and Neel: New Inherited Abnormality of Hemoglobin. Blood, 6: 1340, 1951.
9. Itano, H. A.: Proc. Nat. Acad. Sc., 37: 775, Dec. 1951.
10. Von Korber: Inaurg Diss. Dorput, 1866.
11. Leeks and Wolman: Fetal Hemoglobin in Humans. Am. J. Med. Sc., 219: 684, 1950.
12. Singer; Chernoff; Karl and Auriz: The Interrelationship of Type S and F Hemoglobin in Sickle Cell Anemia. Blood, 7: 47, 1952.
13. Jungblood, J. J.: J. Physiol., 92: 229, 1938.
14. Darrow; Nowakausky and Austin: Arch. Path., 30: 873, 1940.
15. Hock; Beaver and Holiday: J. Biochem., 40: 374, 1951.
16. Itano, H.: Human Hemoglobins. Science,117 : 99, 1953.
17. Parter and Sanger: J. Biochem., 42: 287, 1948.

18. Ibid, Ref. 15.
19. Itano; Pauling; Singer and Wells: Sickle Cell Anemia, a Molecular Disease. Science, 110: 543, 1949.
20. Terutz and Mitchison: Hemoglobin in Sickle Cell Anemia. Nature, 166: 677, 1950.
21. Negro and the Sickle Cell. J. Biol. Chem., 187: 22.
22. Pauling; Itano; Wells; Schroeder; Kay; Singer and Corey: Science, 111: 459, 1950.
23. Ranny; Larson and McCormack: J. Clin. Investigation, 32: 2, 1953.

CARDIOSPASM IN CHILDREN. W. L. Palazzo. (J. M. Soc. New Jersey, 52:569-571, Nov. 1955).

The author presents histories of two children with cardio spasm or achalasia whom he observed during the last four years. The condition is uncommon but is not rare. The symptoms of cardiospasm are those of obstruction at the cardia. In the newborn infant, vomiting or regurgitation of uncurdled milk is noted. In older children vomiting of undigested food is suggestive. This may be intermittent. There is generally poor nutrition and a failure to gain weight. The sensation of hunger is usually preserved. Recurrent lower respiratory infections occur as food material overflows from the filled esophagus into the tracheo-bronchial tree. The roentgen findings are those of constriction of the esophagus at the cardia. Fluoroscopically there may be observed intermittent relaxation of the cardia, allowing small amounts of barium to pass into the stomach. Mild cases may show only slight dilatation of the esophagus. Later cases may show marked dilatation and elongation, with loss of peristaltic action. Filling defects in the esophagus are often seen, representing retained solid food material. Plain chest films may show an air and fluid containing sac in the mediastinum, projecting usually into the right side of the chest when the esophagus is more dilated and elongated. The first of the two children presented here had a relatively early case with only moderate dilatation of the esophagus. The second case was of longer duration, showing a markedly dilated esophagus, with bronchopneumonia resulting from the spillover of ingested material into the tracheo-bronchial tree. Cardiospasm should be thought of as a possible cause of vomiting in children, and children with frequent respiratory infections should be subjected to esophagography to investigate the possibility of a spillover syndrome associated with cardiospasm. —*J. A. M. A.*

THE DEVELOPMENTAL MECHANICS OF HEART MALFORMATIONS

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Some twenty-five years ago heart malformations were studied by only a few pathologists, who were interested in problems of malformations in general. Severe cases seemed hopeless and died early, and milder formations were more or less regarded as curiosities in older people. This situation has changed since many congenital heart diseases are remedied by surgery. New diagnostic methods have been developed and every cardiologist, pediatrician and surgeon is now interested in this field which many consider a new chapter in medicine.

Explanations for the development of heart malformations have changed in the course of time. Senac, in 1749, called them "play of the intelligence formatrice," probably meaning the same as "vitium primae formationis." Meckel, in 1802, formulated a theory in his book, "De Cordis Conditionibus Abnormibus," that we deal here with a fixation on earlier regular formations, such as the hearts of lower animals which he thought were copied by the malformations. He was primarily interested in the combination of pulmonary stenosis and septal defects, a combination which has been studied by Morgani and by Hunter. Later, the role of endocarditis in heart diseases was understood and many authors tried to find a connection between heart malformations and fetal endocarditis. H. Meyer, the leading pediatrician one hundred years ago, claimed that the combination of pulmonary stenosis and septal defect is caused by fetal inflammation of the heart, contradicting Heine, Halbertsma and others, who have specifically termed this combination a primarily pathological anlage. Endocarditis of the fetus as the cause of malformations was supported by many pathologists even recently, and is probably the cause of some rare congenital heart diseases. The reason for this was that the right side of the heart is more often affected since it receives the blood first from the umbilical veins and is, therefore, the first to be infected. This was disproved by many authors; first by Rauchfuss; later by Hansemann, and many others, who described pregnant

mothers with endocarditis, the child showing the same pathological picture as the mother, namely, endocarditis of the mitral valve. I also saw, many years ago, the newborn child of a mother, who died at childbirth from acute endocarditis. The child had a severe endocarditis of the mitral valve.

It is now nearly one hundred years ago that Rokitansky published his famous book, "The Defects of the Septa of the Heart." This closed the discussion regarding endocarditis, false anlage, or imitation of animal hearts. He was the first to use exact embryological observations and explained septal defects as well as abnormal position of the large vessels as caused by a wrong torsion of the septum trunci. He was the first to look for mechanical causes, and explained many different theories from one point of view. Development of embryology has shown that Rokitansky's concept was not entirely correct. Born and Hiss, especially, have shown that the anterior part of the ventricular septum is not the source of the last occlusion of the incomplete septum by growing to the right side upward, but, rather, that the last building stone comes from the septum trunci. These findings contradict the base of Rokitansky's genial conception. Vierordt wrote that though it was known that Rokitansky's theory was not correct, there was nothing better to replace it.

This was the situation when a boy died in our hospital in Vienna, who showed a dextrocardia, extremely severe cyanosis, and, at autopsy, a very rare, severe heart malformation. There was one large ventricle only which showed some small muscle ridges, the aorta was very large, displaced far to the right side, the arteria pulmonalis was very small. This isolated transposition of the aorta with stenosis of the arteria pulmonalis, and a nearly complete lack of the ventricular septum does not agree at all with Rokitansky's theory. We know it was at that time the Viennese anatomist, Alexander Spitzer, published some new theories regarding the embryology of the normal heart. We called on him in his laboratory and asked him to examine this heart and give us an explanation. His answer was very simple: "I am an anatomist, I never have seen a heart malformation, and have not heard about them since my student days. However, since you have gone to the trouble of coming to see me, I can look at it." After a lengthy study of the heart, he said: "I think I can give you an explanation

as to what happened to the heart." This was the birth of Spitzer's famous theory on heart malformations.

Spitzer started his theory from a teleological point of view. Lung breathing achieves its purpose of best oxygen supply to the body only with cross circulation through a divided heart, and accomplishes it finally. But his teleology had no metaphysical basis; he thought that mechanical conditions finally led to functional advantage. His teleology brings to mind a statement by Bruecke, who once said that teleology plays to physiologists the same role as a beautiful woman of bad reputation—he cannot live without her, but does not like to be seen with her in public.

Spitzer's ideas are based on the change which takes place when animals leave their abode in the water and creep to land. They need a much larger amount of oxygen. The blood leaving the gulls in fish is well oxygenated; this advantage is lost in higher animals when they develop lungs as an organ with increased surface for better exchange of oxygen and carbon dioxide. Development of lungs is parallel with an increase of the blood volume passing the lungs. Spitzer discussed in detail how blood pressure, pulse pressure, increased blood volume dilate the vessels, sometimes elongating, sometimes even shortening them. The spores, especially, between two vessels receive a growth stimulus from increased pressure, and grow slowly in the direction of the heart. Even the appearance of cushions in the heart tube could be partly the result of tension in the increasing and dilating tube.

All these discussions about mechanics are interesting but only as an introduction to the new theories regarding the development of the normal human heart. It cannot be doubted that the body's oxygen supply is best obtained when blood is oxygenated in a special organ, the lungs. The blood then returns to the heart, goes from the heart to the periphery delivering the oxygen, returns to the heart, and back to the lungs for renewed oxygenation. For this purpose we need a septum which divides the heart into two halves, one with oxygenated, the other with venous blood. This is achieved finally in birds and mammals, but lower animals have an incomplete separation. Reptiles have two aortae, one originating in the left ventricle, the other in the right ventricle. They, therefore, supply only the head with fully oxygenated blood.

Suppose that we were the architects who have to construct a

complete separation of the two halves of the heart in a straight tube, how would we go about it? A simple septum would divide the heart, but not supply the necessary switch of the blood. Then too, any rotation of the heart would not improve the situation. The simplest way would be to have one of the large vessels originating not directly from the heart, but from the neighboring vessel, and complete the separation after the rotation has taken place.

Spitzer has shown that this is exactly what takes place in the course of heart development. The occurrence is similar in the ontological as well as in phylogenetic development. But he stressed many times that this similarity is the result of similar mechanical conditions and not a mystical imitation of lost features. He proved from embryological observations, as well as from findings in the developed heart, that the heart really performs in an early stage of development a rotation around its axis. The degree of rotation differs in the various types of animals. This rotation itself works as a stimulus for the growth of the septum, but is also responsible for the occlusion of the right ventricular aorta. This rotation takes place at a time when both auricles are not parallel, but one behind the other.

The right ventricle of reptiles shows two muscle ridges which in systole separate the outflow of the right ventricular aorta from the outflow of the arteria pulmonalis. In diastole both streams are mixed. These two ridges are not present in the heart of mammals or birds. Spitzer has shown that they do not disappear completely, but are reduced only to two very insignificant ridges in the human heart, which sometimes are visible in the heart of the newborn only, and are called the crista supraventricularis and trabecula septomarginalis. Spitzer has shown that the crista develops from the proximal cushion C, for which no descendant has been known in human embryology.

Spitzer's theory about the physiological development of the human heart deviates from the older concept. It was always known that the large vessels show a rotation, one around the other. Spitzer has shown that this is the result of a rotation of the heart itself. This rotation has many mechanical results, such as the growth stimulus to the septa and the occlusion of the right ventricular aorta, as well as the diminution of the strong muscle ridges in the right ventricle to the insignificant crista and trabecula.

The first heart malformation which we showed him was, fortunately, the rare combination of an aorta transferred to the right ventricle, a large defect of the septum and a stenotic arteria pulmonalis. Spitzer pointed out that there was a marked niche, where normally the left ventricular aorta originates. The present aorta was located where, in reptiles, the right ventricular aorta begins. He also showed us the two muscle ridges which corresponded to crista and trabecula, but were much more marked than usual in the human heart. He, therefore, explained our specimen as a malformation which developed because the conus of the left ventricular aorta closed and the conus of the right ventricular aorta remained open. We have published a description of this heart with Spitzer's explanation titled, "Transposition of the Aorta or Persistent Right Ventricular Aorta."

The next heart which we brought to Spitzer's attention was the more common type, which is usually called tetralogy of Fallot: a severe pulmonary stenosis, a septal defect and a large aorta riding over the septal defect. The heart was incompletely opened as we asked our pathologist, Prof. v. Wieser, to leave it for Spitzer, so that no parts would be destroyed which later could prove to be important. The large vessels, therefore, were not opened. Spitzer examined the septal defect, the large riding aorta and thought that this malformation could be the result of fusion of the two conuses of the right ventricular and the left ventricular aorta. He added: "If my theory is correct, then the arteria pulmonalis must have two cups only." The artery was cut and there were the two cups. This prophesy was such a surprise to me that I definitely believed in his theory and tried to make it as widely known as I could.

Spitzer knew that the cups in aorta and arteria pulmonalis develop from the distal, horizontal, endothelial cushions, which also produce the septum trunci. Cushion 1 and 3 combine in mammals to build the septum and separate the two vessels. There are three remaining parts of the cushions in both vessels, producing three cups in aorta and in arteria pulmonalis. The division of the truncus in reptiles differs in that three vessels are produced, the arteria pulmonalis and two aortae. The two septa develop, dividing the truncus in three parts, but leaving two cups only for every vessel. On the phylogenetic course, the septum of the reptile shifts from cushion 2 to 3. In our malformation, therefore, Spitzer as-

sumed a fusion of the two aortae, with one truncus septum only. This leaves three cups for the large aorta, two cups only for the small arteria pulmonalis.

Spitzer asked the author to publish his theory regarding the human's two hearts in a paper on heart malformations which was given consideration at that time. He himself published his theories on heart malformations years later after intensive study of every heart malformation he could obtain. The primary thought of this new concept regarding the developmental mechanism leading to heart malformation is that the normal rotation of the heart sometimes is not completed. Spitzer termed this detorsion. The normal rotation is a mechanical stimulus for the growth of the septum and occlusion of the right ventricular aorta. Detorsions, therefore, leaves the septum incomplete and opens the conus of the right ventricular aorta. Some details of rare heart malformations cannot be explained by this simple fact only and Spitzer has shown that sometimes detorsion is combined with partial situs inversus. He deplores the suggestion that this occurs when the primary heart tube rotates in the wrong direction. Such a turn would not only change the right and left side, but also front and back. But the anterior and posterior sites have not changed with the inverted parts which sometimes, but very rarely, are found as a mirror picture of the norm. These two concepts could account for a large series of heart malformations. The variety of findings corresponds to the endless possibilities of the degree of detorsion.

In the course of detorsion, the intraventricular septum becomes smaller and smaller, and crista, and trabecula grow larger and larger, until, finally, a stage is achieved where the normal septum has disappeared and the two ridges are large enough to simulate incomplete septum. This suggests a transposition of the arteria pulmonalis to the left ventricle, because it is left from the simulated septum. Actually, the vessel remains in its place, but the true septum has disappeared and a new ridge produced on the other side of the vessel. Spitzer divides the detorsion into four stages, which are responsible for more and more severe malformations. He has shown also that the mechanical conditions during the development of heart malformations differ from those in lower animals. When detorsion opens the conus of the right ventricular aorta, it may also close the conus of the left ventricular aorta.

Spitzer shows the relation of heart malformations to detorsion in four pictures, the first of which shows the normal conditions. We see a cut through the upper part of the ventricles. It is an orthogenal projection of the ventricular structures onto the plane of the ventricular base. We see the normal localization of the septum with the pars membranacea; the aorta and tricuspid valves are located in the left ventricle. We see the papillary muscles neighboring the septum. The right ventricle contains the arteria pulmonalis, the tricuspid valve, which lies near the trabecula. We see the small crista, and between them the depression, which Spitzer has described in the normal human heart as the closed conus of the right ventricular aorta.

Spitzer's Type I. This is generally called tetralogy of Fallot. The difference from the norm is the large aorta which covers the location of the normal left ventricular aorta as well as the conus of right ventricular aorta. The arteria pulmonalis is very small and contains two cups only. The septum between ventricles shows a defect near the pars membranacea. The crista supraventricularis is somewhat more marked than normally.

Spitzer's Type II. We have here a transposition of the aorta to the right ventricle. The arteria pulmonalis is small, has two valves, but is located normally. The crista is well marked. The septal defect is quite large, but the septum clearly visible. The crista is located as usual between arteria pulmonalis and right ventricular aorta.

Spitzer's Type III. This is the old, great puzzle of transposition of both large vessels into the "wrong" ventricle. Here the anterior part of the septum is not developed and, therefore, the large crista simulates the anterior part of the septum. The aorta pulmonalis is at its normal place, but is termed transposed because the ventricles are not divided by the true septum in right and left, but partly by the septum and partly by the crista. The arteria pulmonalis is practically always small with two valves. The position of the papillary muscles helps to localize the septum verum.

Spitzer's Type IV. This suggests the transposition of both large vessels and transposition of the tricuspid valve so that the small right ventricle contains the aorta only. The septal defect alone makes circulation possible. Here detorsion is so severe that the whole septum is not developed; crista and trabecula are well

developed, and impress as incomplete septum. Papillary muscles mark the position of the true septum far to the left of the present ridges which impress as septum. The aorta, again, is the right ventricular aorta; arteria pulmonalis and tricuspid and mitral valves are in their place but impress as transposition, as they are left from the present ridges. The right ventricle is very small, the arteria pulmonalis large, with three normal cups.

Spitzer has given many indications which prove the degree of torsion in these various forms. One of the most marked features is the position of the coronary arteries which also rotate normally, and show more and more detorsion in the different types of malformation. Farber and Harris have published a report on many heart malformations from Spitzer's point of view, and have confirmed Spitzer's theory that in their cases the coronary arteries indicated more and more "detorsion" in their position, in line with Spitzer's types.

Spitzer does not call his theory a phylogenetic one, which is a fixation of the heart on the level of reptiles or something similar. He claims that the anlage of the heart is the same in all animals, and that mechanical forces cause different results. The torsion, in the course of development, causes closing of the right ventricular aorta. Detorsion does not change a human heart into a reptile heart, it only opens the aorta which "anlage" was always there. The conus of this second aorta is opened and is connected with the common ascending aorta. We do not deal with the transposition of a vessel, a process which would be completely foreign and contrary to the normal formation of the heart. We have here a preordained, latent phenomenon becoming manifest.

Spitzer described subgroups in between his types, especially with the transposition of both vessels, where the septum may be developed differently or even be complete. A subgroup between the norm and type I, shows the shifted aorta, the septal defect, but a normal arteria pulmonalis, the so-called "Eisenmenger" complex. Also Doerr explained two heart malformations as subgroups between Spitzer's types.

Only a single theory on malformation has been published since Spitzer's papers were released, the theory of Pernkopf. He was the leading nazi at the Vienna University, became dean of the Medical School when Hitler took over in Austria, and was an old

antagonist of Spitzer. He claimed that malformations are caused by partial situs inversus combined with abnormal absorption of the bulbus. Spitzer criticized Pernkopf's theory in a very aggressive manner. He had discussed situs inversus in his theory, and claimed that Pernkopf had "stolen" that part of his theory from him just as he had "taken over" the importance of the crista, the appearance of the right ventricular aorta, etc. Everyone knows that the embryo, as well as the reptile, have a bulbus which is not present in the human heart. Pernkopf's deductions regarding the influence of this disappearance in malformations is nonsense. Spitzer discussed those parts of Pernkopf's findings which were not previously described by himself many times with the author, who was in accord with Spitzer. Nor does the author agree with the surprising position of the two American pathologists, Lev and Vass, who translated, in a very admirable way, Spitzer's work They introduced their book with a eulogy, included his photograph and called the late Spitzer a great man. However, they end with a critique in which they destroy the basis of Spitzer's theory, claiming that it had to be adapted to Pernkopf's new findings in embryology. They deduced that "the concept of detorsion as the cause of transposition or a change in the first phase of the development of the heart seems unlikely; instead of beginning the theme of the abnormality in transposition with detorsion it begins with lack of proper formation of the new ridge 3 B". This perhaps stems from an old publication by Lev, and contradicts Spitzer's entire theory. They also omitted, in their translation, Spitzer's case records wherein he showed in a marvelous way the increasing detorsion.

Is Spitzer's theory able to explain every type of heart malformation? Far from it. Spitzer himself enumerates a list of malformations which are caused by an arrest of development so that some parts of the heart remain in a state which are normal in an earlier phase of development, such as foreamen ovale, atrial septal defect, ductus aperture.

In general, heart malformations can be divided into three groups: (1) abnormal connection between right and left; (2) anomalies of the vessels and valves; and (3) repeatedly occurring combinations. The abnormal connection may be seen between the ventricles (defect of the ventricular septum of Maladie de

Roger), between the auricles (defect of the auricular septum from an open foramen ovale up to the persistence of the foramen primum), or between the vessels (truncus communis as well as open ductus arteriosus). Ventricular septal defects are sometimes the first stage of detorsion. Spitzer begins his series of heart malformations with one heart taken from a paper by the author, where mild detorsion has not had any other sequelae as incompleted septum with a minimum dislocation of the aorta. Some ventricular septal defects have to be explained in another way. Those in mongoloids will be mentioned later. However, there is a special type of ventricular septal defects, localized in a much lower part of the septum, and located, as Shato claims, near a partition of the conductive system, in the muscular part of the septum. They were once called "perforation defects," because it was thought that they were the result of a perforation of the septum by blood pressure. Moenckeberg has shown that such defects are very common in the newborn, but rare later, and thinks that they, more or less by chance, remained open between the muscle fibres, and grow out spontaneously, when contraction of the muscles keeps them closed. I have explained in this way a very astonishing experience which I had many years ago. A famous pediatrician had twin daughters. One, at birth, had a very loud systolic murmur over the heart such as is found in small ventricular defects. Once, when she was some weeks old, we tried to observe the heart under fluoroscope. The heart seemed unusually enlarged. The child cried vehemently, became quite red in the face. Suddenly, while under observation, the heart became normal in size, the murmur disappeared, and the girl never again showed any sign of heart disease and is now the healthy mother of two children. Hochsinger has explained, in the same way, some observations on loud murmurs which disappeared suddenly.

The open ductus arteriosus is a much discussed chapter. It is not correct to call it a congenital heart disease inasmuch as it closes after birth. Most surprising, however, is the fact that it is found so often in children of mothers who had German measles during pregnancy. How can an infection months before birth prevent the normal closure of the duct after birth? There have

been three theories about the mechanism which normally causes the occlusion of the duct. Haberda claimed that the well developed muscles of the duct close it by active contraction. Strassmann explains the closure in another way. The ductus leaves the arteria pulmonalis in an oblique angle. When the arteria pulmonalis after birth is dilated by expansion of the lungs, the angle between ductus and artery decreases and the spore between the vessels acts as a sluice which closes the ductus automatically. A third explanation is a clot often found in the ductus as the cause of circulatory inhibition. Probably all three mechanisms play their role normally. The tendency to close must be quite powerful; there are cases on record where children died because the ductus was the only way open for circulation in severe malformation. A new theory by Haring is based on the assumption that ductus aperture is never combined with an open foramen ovale and claims that premature closure of the foramen ovale causes right ventricular hypertrophy and increased pressure which prevents the normal closure of the duct.

Anomalies in the valves and vessels may occur in any one of them. Fetal endocarditis seems to be the best explanation for some of them, such as is occlusion of the arteria pulmonalis. The author once described a heart in which circulation was possible only through the broad ductus, the right ventricle being a round, thick muscle with practically no lumen, the left ventricle, enormously enlarged, encasing the right ventricle like a shell. Such malformations may be the result of early fetal endocarditis. Stenosis of the arteria pulmonalis with underdeveloped small artery are probably better explained by Spitzer's theory.

Malformations of the mitral valve are rare. Stenosis of the mitral valve, combined with a defect of the auricular septum, are described as Luttembacher's syndrome, a condition which at first does not show severe signs of circulatory distress, until, suddenly, the heart fails, enlarges enormously, and both auricles and the right ventricle become so distended that we have the largest hearts ever seen in man, a really bizarre monstrous corbovinum. It could be suspected that stenosis causes in the early stages of development an increase in pressure in the left auricle, which prevents the closure of the auricular septum. Dressler and Roesler

have shown that this is impossible as the auricular defect is the first to develop. An explanation of this combination is, therefore, lacking.

The tricuspid valve shows sometimes a very different type of malformation, a stage of underdevelopment with the clinical signs of severe tricuspid regurgitation. This malformation is often called Ebstein's disease, as it has been described by Ebstein, although the first case of this type was described by Otto. A mechanism leading to this malformation has not been proven.

Stenosis of the aorta occurs on two different points, on the origin of the aorta in the heart, the conus-stenosis, or, on the descending aorta near the origin of the ductus, the so-called isthmus stenosis or coarctation. The first malformations are nearly always combined with severe malformation of the heart and are quite rare. Isthmus stenosis has been divided by Bonnet into the two types; (1) proximal to the open duct (infantile type); (2) distally with a closed duct (adult type). The infantile type is always combined with severe anomalies of the heart or malformations of the whole aorta. The adult type found a marvelous explanation by the great clinician Skoda. He claims that the muscles of the ductus disappear after its occlusion and the whole duct changes to connective tissue. This process sometimes does not stop at the level of the aorta but builds a ring at the aorta itself. This, at first, does not impair circulation, but later, when the aorta increases in size, this connective tissue band does not grow well and causes stenosis; circulatory troubles start slowly, and there is mostly time for the development of collateral passways, primarily the arteria mammaria interna, then the arteria circumflexa on the outside of the scapula. Its pulsation is one of the characteristics of this disease, together with notching ribs caused by dilated arteries. During puberty the heart and the aorta enlarge very quickly and usually it is at that age that troubles begin. The localization of the stenosis explains the leading symptoms in this condition, the high pressure in the arteria radialis and the low pressure, even the pulse which is not felt in inguine or on the back of the feet. In some cases the ductus originates between the origin of the left carotis communis, and the left subclavian artery, and then, there is a marked difference between right and left radialis pulse. Skoda's theory explains, also, why

circulation is primarily not much impaired; collateral vessels have time to develop, trouble starts at time of puberty when heart and aorta grow rapidly, but the stenotic part remains small.

Skoda's theory was often criticized. Edwards and co-workers, Friedberg and others, claim that they could not find the pathological tissue ring in coarctation.

Friedberg proposed a new theory regarding isthmus stenosis. He claimed that in the fetal circulation, well oxygenated blood from the vena cava inferior goes directly to the aorta, providing blood to the head and arms. The blood of the superior vena cava goes through the foramen ovale to the arteria pulmonalis and the duct, the descending aorta, supplying the lower half of the body with blood. The part of the aorta from the origin of the left subclavian artery to the duct, called isthmus, is at this time unimportant for circulation and remains small. At birth, the lungs need more blood, which is diverted from the duct to the lungs. The lower extremities have to be provided with blood from the aorta, the duct becomes useless and closes. It remains open only while the isthmus is extremely small, or the pressure from the left ventricle is very weak. This explains Bonnet's infantile type with open duct, but it does not explain isthmus stenosis by closed duct, Bonnet's adult type. Doerr prefers to divide isthmus stenosis into the obliterine and the hypoplasiogene types, unquestionably less confusing than Bonnet's older nomenclature.

Skoda's explanation of the influence of the closing of the duct on isthmus stenosis by traction and by a change of tissue in the aorta does not seem to be completely refuted. It is self-evident that it has no relation to cases of the infantile or hypoplasiogene type. But for patients with a closed duct the slow development of the stenosis, the increasing collateral circulation, the start of heart failure after puberty has to be explained. Even Skoda knew that there very often is not a connective tissue ring in the aorta. He spoke about traction by the duct as the inhibiting cause of development of the aorta at time of birth to the normally sized aorta of the adult.

From Spitzer's theory, it is very interesting to note that not only the conus of the right ventricular aorta may open, but also the right aorta itself. Cases of a right aorta, without any clinical symptoms, and only a peculiar x-ray picture are not too rare.

In other patients both aortae or at least partly doubled aortae are present, which sometimes builds a loop around the esophagus, causing difficulties in swallowing and recurrent paresis, etc. Surgery for these cases seems to be the simplest and most impressive correction of malformations of the circulation. Gross was the first to perform this operation. Normally the left 4. gill artery develops to form the aorta, the right to become the right subclavia. Anomalies and aberrations of the right subclavia are by far the most common abnormality of arterial distribution, a fact which I stressed twenty-five years ago.

Anomalies of the development of the large vessels, the right aorta and the right 6 arch to build a duct, anomalies in the origin of the carotic artery have been described by Wilson and Warkany in offsprings of rats fed on vitamin A free diet.

Mongoloids furnish a special chapter in our study of heart malformations. Many mongoloids have heart malformations. Benda claimed that nearly 70 per cent of the newborn have abnormal hearts, but the severe cases die early. We found among the 280 mongoloids at Wrentham, 35 per cent (68) had loud murmurs. The most common malformations are defects of the ventricular or of the auricular septum, or both. Tetralogy of Fallot and pulmonary stenosis are rare, and the author does not know one mongoloid with a complete transposition of both large vessels. An overwhelming percentage of the severe malformations in mongoloids is the ostium atrio-ventriculare commune, where the mitral and tricuspid valves are so underdeveloped that there is no separation of atria and ventricles. The septum between the ventricles also is missing, and generally, only remnants of the auricular septum are present. We have often found a one-chambered heart. The clinical signs are astonishingly minor. Often there are no murmurs at all; no cyanosis; a mildly enlarged heart. But in time of stress, respiratory infections, and such, these children may die very suddenly.

Maud Abbott, a leading student of heart malformations, wrote in her "Atlas on Congenital Heart Diseases" about this malformation, that its outstanding feature is the fact that it has been found in mongoloids only, a statement which calls for an explanation.

The fact that the more common severe malformations are seen

rarely in mongoloids, whereas the severe malformation typical for mongoloids is not seen in other children, seems to confirm that different developmental mechanisms are at work here. Spitzer's series of malformations may sometimes also occur in mongoloids. But the ostium atrio-ventriculare commune must be based on conditions of mongolism.

The heart develops from a straight tube, which contains two series of endothelial cushions. The proximal, longitudinal cushions are called A, B and C. Spitzer has shown that C is the source of the crista supraventricularis. These cushions develop in the so-called first stages of heart development, and build the ventricular septum, part of the mitral and tricuspid valve, and a part of the auricular septum. The second row of cushions are the distal, horizontal cushions, 1, 2, 3 and 4, which later develop into the cups in aorta and arteria pulmonalis as well as into the truncus septum. These parts develop in the so-called second stage of heart development, according to Tandler's division.

We see, therefore, that the parts which evolve in the first stage of development are those parts of the heart which do not develop or remain at least underdeve'oped in the ostium atrio-ventriculare commune.

Ingalls explains mongolism as caused by any damage to the fetus in the first weeks of development which interferes with normal nutrition, especially with an insufficient oxygen supply. Benda thought that at this stage, a growth stimulus is missing, probably normally produced by the maternal pituitary. Any such damage to growth at this early stage of development could also interfere with the normal development of the proximal cushions leading to septal defects, when the inhibition is mild, and producing the ostium atrio-ventriculare commune when severe.

The answer to the question as to what primarily causes heart malformations is not known as yet, but we have obtained some hints from recent research. Roesler claimed that consanguinity is higher in parents of children with heart malformations than in the normal population. Genetic determination in some cases could be possible, especially the open ductus which have been found in several members of the same family. Campbell, McKeown and others have observed families of children with heart malformation, and found, in rare cases, several patients in one family. In

other cases, diseases suffered by the mother during pregnancy were reported. Roesler also found a high percentage of alcoholic parents. Syphilis does not seem to play a role in his cases. Severe heart malformations are overwhelmingly isolated findings in a family and cannot be explained by genetic determination. Heart malformations probably have the same cause as other malformations.

We have learned, in the last decades, the danger of damage to the pregnant mother in regard to the normal development of the offspring. In animal experiments, malformations have been produced by one-sided nourishment (Warkany, Hogan), by insulin injections (Duraiswani), by oxygen deprivation (Ingalls), by x-ray radiation. In man, our interest in embryopathy started with malformations found in pregnant women with German measles (Gregg). The danger of x-ray radiation was known long ago. For centuries malformations were connected with excitement, fear, accidents to the pregnant mother. We would hesitate, today, to call such concepts superstitious. We have learned that not only German measles, but every virus infection, probably other diseases as well, may be followed by development of a malformed offspring. Damage of another type may also play a role, specifically, attempted abortion. We have learned that the type of malformation depends in part on the time as well as on the type of damage. Early damage leads to malformations, later damage to cerebral injury. Heart malformations are possible when damage to the fetus occurs before development of the heart is completed. We have seen that heart malformations may differ according to the time of inhibition of development.

Most of the congenital malformations are probably determined in the first 6 to 8 weeks of gestation. Animal experiments often enable us to answer questions with exactitude. In some experiments of damage to pregnant animals, heart malformations were produced. The best known and analyzed findings are those of Wilson and Warkany, who produced septal defects and abnormal localization of the aorta in rats born to animals kept on a vitamin A low diet. Wolff has described heart malformations following x-ray radiation, and Buechner the condition following low oxygen supply to pregnant animals.

We hope that further studies will supply us with more material towards an explanation of how heart malformations develop. This might even lead to prophylactic measures to prevent such malformations.

REFERENCES

Abbott, M.: Atlas of Congenital Cardiac Disease. Am. Heart Ass., New York, 1936.
Benda, C. E.: Research in Congenital Acromicria (Mongolism) and Its Treatment. Quart. Rev. Pediat., May 1953.
Benecke, W.: Ueber Herzbildung und Herzmissbildung als Funktionen primaerer Bildungsformen. Beitr. z. path. Anat. u. z. allg. Path., 67.
Bonnet, M.: Sur la lesion dite stenose congenitale de l'aorte, dans la region de l'isthme. Rev. de mé.d, 23:108, 255, 335, 418, 481, 1903.
Born: Beitraege zur Entwicklungsgeschichte des Saeugetierherzens. Arch. f. mikr. Anat., 33, 1889.
Buechner, F.: Exp. Entwicklungsstoerungen durch Sauerstoffmangel. Klin. Wchnschr., 24:137, 1946.
Campbell, M.: Congenital Heart Disease. Guy's Hosp. Gaz., 60:159, 1946.
Doerr, W.: Zwei weitere Faelle von Herzmissbildung. Ein Beitrag zu Spitzer's phylogenetischen Theorie. Virchows Arch. f. path. Anat., 301:668, 1938.
Doerr, W.: Pathologische Anatomie typischer Grundformen angeborener Herzfehler. Monatschr. f. Kinderh., 100:107, 1952.
Dressler, W. and Roesler, H.: Verhofseptumdefekt Kombiniert mit Mitralstenose und aurikulaerem Leberpuls. Ztschr. f. klin. Med., 112:121, 1930.
Duraiswani, P. K.: Insulin Induced Skeletal Abnormalities in Developing Chicken. Brit. Med. J., 12:384, 1950.
Ebstein, W.: Ueber einen sehr seltenen Fall von Insuffizienz der Valvula tricuspitalis. Arch. f. Anat., Physiol. u. wissensch. Med., 238, 1866.
Edwards, J. E.; Christensen, N. A.; Clagelt, O. C. and McDonald, J. R.: Pathological Considerations in Coaretation of Aorta. Proc. Staff Meet., Mayo Clin., 23:324, 1949.
Friedberg, C. K.: Coaretation of Aorta; A New Theory As To Its Pathogeneais. J. Mt. Sinai Hosp., 8:520, 1942.
Gregg, N. M.: Tr. Ophth. Soc. Australia, 3:35, 1942.
Gross, R. E.: Surgical Relief for Tracheal Obstruction from a Vascular Ring. New England J. Med., 233:586, 1945.
Haberda, A.: Die foetalen Kreislaufwege der Neugebornen und ihre Veraenderungen nach der Geburt, Wien, 1896.
Haring, O. M.: Patency of Ductus Arteriosus After Birth; A New Theory. Dis. of Chest, 27:1, 1955.
Harriss, J. G. and Farber, S.: Transposition of Great Cardiac Vessels with Special Reference to Phylogenetic Theory of Spitzer. Arch. Path., 28:421, 1939.
Heinrich, H.: Die Geschichte der angeborenen Herzkrankheiten. Dusseldorfer Arbeiten v. Geschichte der Medizin 1. Dusseldorf, 1927.
His, W.: Anatomie menschlicher Embryonen, Leipzig, 1880.
Hochsinger, K.: Ueber das Zyanoseproblem bei den angeborenen Herzfehlern der Fruekindheit. Wien. med. Wchnschr., 88:41, 69, 93, 147, 181, 207, 235, 261.
Hogan, A. G.; O'Dell, B. L. and Whitley, J. R.: Maternal Nutrition and Hydrocephalus in Newborn Rats. Proc. Soc. Exper. Biol. & Med., 74:293, 1950.
Hunter, W.: Medical Observations and Inquiries by A Society of Physicians in London, 1783.
Ingalls, Th. H.: Etiology of Mongolism. Am. J. Dis. Child., 74:147, 1947.
Ingalls, Th. H.; Curley, F. S. and Prindle, R. A.: Experimental Production of Congenital Anomalies; Timing and Degree of Anoxia as Factors Causing Fetal Deaths and Congenital Anomalies in Mouse. New England J. Med., 247:758, 1952.
Ingalls, Th. H.; Curley, F. C. and Prindle, R. A.: Anoxia as Cause of Fetal Death or Congenital Defect in the Mouse. Am. J. Dis. Child., 80:34, 1950.
Lev, M. and Vass, A.: The Architecture of Normal and Malformed Hearts, 1951.
Lev, M. and Saphir, O.: A Theory of Transposition of the Arterial Trunk Based on the Phylogenetic and Ontogenetic Development of the Heart. Arch. Path., 39-172, 1945.
Liebur, A. A. and McFerland, W.: Corrected Transposition and Persistent Rudimentary "Right" Aorta as Evidence in Support of Spitzer's Theory. Arch. Path., 32:356, 1941.
Linzenmeier, G.: Der Verschluss des Ductus arteriosus nach der Geburt des Kindes. Ztschr. f. Geburtsh. u. Gynäk., 76:217, 1915.
Luttembacher, R.: Stenose mitrale et communication interauriculaire. Arch. d. mal du coeur, 9:237, 1916.
Mautner, H.: Zur Entwicklungsgeschichte, Pathologie und Klinik angeborener Herzfehler. Jahrb. f. Kinderh. 96:123, 1921.
Mautner, H. and Loewy, M.: Transposition der Aorta oder Persistenz einer rechtskammerigen Aorta. Virchows Arch. f. path. Anat., 301:668, 1938.
Mayer, J. B.: Zur Aetiologie angeborener Herzfehler. Monatschr. f. Kinderh., 100:146, 1952.

Meckel, J. F.: Handbuch der pathol. Anatomie, Leipzig, 1812.
Meyer, H.: Ueber die transposition der aus dem Herzen hervortretenden grossen Arterienstaemme. Virchows Arch. f. path. Anat., 12:264, 1857.
Meyer, H.: Ueber angeborene Enge oder Verschluss der Lungenarterienbahn. Virchows Arch. f. path. Anat., 12:497, 1157.
Moenckeberg, I. G.: Beitraege zur Entwicklung des Atrio-ventrikular—systems und zu seinem Verhaeltniss bei schweren Missbildungen des Herzens. Zentralbl. f. Herz. u. Gefässkr., 7:273, 1915.
Moenckeberg, I. G.: In Handbuch d. Path. von Henke-Lubarsa, 2:1921.
Morgagni, J. B.: De sedibus et causis morborum per anatomem indigatis, Venetii, 1761.
Otto, A. M.: Lehrbuch der path. Anatomie der Menschen und Tiere, Berlin, 1830.
Pernkopf, E. and Wirtingen, W.: Die Transposition der Herzostien. Ein Versuch der Erklaerung dieser Erscheinung. Die Phononomie der Herzentwicklung. Ztschr. f. Anat. u. Entwcklngsgesch., 100:563, 1933.
Rauchfuss, C.: Die angeborenen Entwicklungsfehler und Foetalkrankheiten des Herzens und der grossen Gefaesse. In Gerhardt's Handb. d. Kinderkr., Tuebinget, 1878.
Roesler, H.: Beitrage zur Lehre von den angeborenen Herzfehlern. II. Untersuchungen zur Actiologiefrage. Wien. Arch. f. inn. Med., 15:496, 1928.
Rokitansky, C.: Die Detekte der Scheidewaende des Herzens, Wien, 1875.
Senac, J. B.: Traite de la structure du coeurs, de son action et de ses maladies, Paris, 1749.
Sato, S.: Ueber die Entwicklung der Atrioventrikularklappen und der Pars membranacea unter Berucksichtigung angeborener Herzmissbildungen. Anat. Hefte., 50:195, 1914.
Skoda, K.: Woch. I. Zeitsch. d. K.K. Ges. d. Aerztein Wien., 2:720, 1855.
Spitzer, A.: Ueber die Ursache und den Mechanismus der Zweiteilung des Wirbeltierherzens. Arch. f. Entwcklngsmechn. d. Organ., 45:686, 1919; 47:511, 1921.
Spitzer, A.: Ueber die Phylogenese der Septierung des Wirbeltierherzens und deren Bedeutung fuer die Erklaerung der Herzmissbildungen. Wien. Wchnschr., 35:561, 584, 1922.
Spitzer, A.: Ueber den Bauplan des normaler und missbildeten Herzens. Virchows Arch. f. path. Anat., 443:81, 1927.
Strassmann, P.: Der Verschluss des Ductus Botalli. Ztschr. f. Geburtsh. u. Gynäk., 6:98, 1901.
Tandler, J.: Anatomie des Herzens, Wien, 1913.
Vierordt, H.: Die angeborenen Hertzkrankheiten. In Nothnagel's Speziellen Pathologie und Therapie, Wien, 1907.
Warkany, J.: Congenital Malformations Induced by Maternal Dietary Deficiency. The Harvery Lectures, 48, 1952.
Warkany, J. and Nelson, R. C.: Skeletal Abnormalities Induced in Rats by Maternal Nutritional Deficiency. ARCH. PEDIAT., 34:375, 1942.
Wilson, J. G. and Warkany, J.: Aortic Arch and Cardiac Anomalies in the Offspring of Vitamin A Deficient Rats. Am. J. Anat., 85.113, 1949.

RUPTURE OF THE LIVER IN A NEWBORN INFANT WITH RECOVERY. J. L. Greaves. (Lancet, 2:1227-1228, Dec. 10, 1955).

In an infant who collapsed 44 hours after birth, intraperitoneal hemorrhage was diagnosed. At laparotomy a tear in the liver was sutured. The infant recovered completely. The author says that rupture of the liver has been found in 1.2% of 2,000 newborn and stillborn infants examined at autopsy. Yet few cases are diagnosed clinically, and so far as he was able to ascertain only six instances of survival have so far been recorded. The case presented here is a further instance of recovery. —*J. A. M. A.*

PEDIATRICS AT THE TURN OF THE CENTURY

From time to time the Archives, which was the first Children's Journal in the English language, will reprint contributions by the pioneers of the specialty over fifty years ago. It is believed that our readers will be interested in reviewing such early pediatric thought.

CAUSATIVE FACTORS OF THE PARALYSES OF EARLY LIFE*

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The paralyses of early life have, as their primary causal factors lesions of the motor tract. These lesions may occur at any point from the cortex to the muscles. They may be due

(1) To congenital defects or malformations.
(2) To lack of development of cortical cells.
(3) To injury to the tract
    from trauma,
    from pressure of hemorrhage or fluid or inflammatory exudate,
    from the displacement of bone, or
    from the growth of neoplasms.
(4) To inflammation of the nervous tissue in brain or spinal cord or peripheral nerves.
(5) To poisoning by bacterial toxins or chemical poisons.
(6) To degenerations of the nerve cells or muscle cells.

These various lesions may reproduce in the young organism the clinical pictures of nearly all the nervous affections of adults in which paralysis is a symptom. However, some of these lesions occur with frequency in the etiology of paralysis in early life and others are of a rarity so great that no instance of them will occur in the experience of a given observer. Therefore, though the consideration of all of these affections would be of great interest from a purely scientific standpoint, from the orthopedic point of view

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and especially from that of a ten-minute paper, it seems more fitting to consider those which occur most frequently and which result in the greatest number of cases of paralysis.

Therefore, beginning with the periphery, we will consider

(1) Primary Muscular Dystrophy,
(2) Obstetrical Paralysis,
(3) Diphtheritic Paralysis,
(4) Pott's Paralysis,
(5) Infantile Spinal Paralysis,
(6) Infantile Cerebral Paralysis,

and dismiss with mere mention the other forms of peripheral paralysis, multiple neuritis due to alcohol or lead, myelitis, syringomyelitis, tumors of spinal cord and brain, brain abscess, hydrocephalus and spina bifida.

Primary Muscular Dystrophy is an instance of primary degeneration of the motor tract, the degeneration affecting the muscles only. Here the paralysis is due to atrophy of the muscle fibers and the consequent loss of power in the muscle as a whole. Previous to, or coincident with this atrophy, there is a deposition of fat in the muscle fibers and an increase of the interstitial tissue of the muscles. The deposition of fat causes the pseudohypertrophy which gives its name to one of the types of this disease. There is no change in the nerves and the late lack of response to faradism is due to loss of contractile muscular tissue and is not a reaction of degeneration. Clinically, paralysis from this affection occurs before the tenth year, occurs most often in boys, has an hereditary tendency and runs in families. The distribution of the paralysis may be of three types: (a) Of the face and shoulder girdle (Landouzy-Déjerine); (b) of the muscles of the back and arms (Erb's Juvenile type); (c) of the muscles of the back and lower extremities (muscular pseudohypertrophy).

Obstetrical Paralysis is a paralysis of peripheral nerves resulting from an injury to these nerves during labor. The characteristic type (upper arm type, or Erb's palsy) is due to injury to the brachial plexus. The seat of injury is commonly the junction of the fifth and sixth cervical nerves. The resulting paralysis affects usually the deltoid, biceps, brachialis anticus and supinator longus—often the supra- and infraspinatus muscles. The brachail plexus

being exposed in the posterior triangle of the neck, pressure from one blade of the forceps, traction on the head to deliver impacted shoulders, traction on an arm, or, as is most often the case, pressure by the fingers in the supraclavicular fossae in the delivery of the after coming head, may inflict a severe laceration to the nerves in this situation on one or both sides.

Facial paralysis and paralysis of the lower extremities may, with great rarity, result from similar trauma to peripheral nerves during labor.

Diphtheritic Paralysis is the result of a multiple neuritis due to the absorption of the toxins of the diphtheria bacillus. It occurs in from 5 to 15 per cent of all cases of diphtheria, but it is rare up to two years of age. It complicates both the mild and the severe types of the disease, but it is more likely to occur with the severe cases, and especially in those cases where antitoxin has not been administered or has been administered late.

The palate is the part first and most often affected. The muscles of accommodation follow and then those of the upper and lower extremities. The nerves of the extremities are probably always affected, as is indicated by the very constant absence of the knee-jerk; but actual paralysis of the extremities occurs, according to the statistics of the American Pediatric Society, only in about 11 per cent of the cases of paralysis. Paralysis of the pharynx, heart muscle and muscles of respiration may occur. The lesion in diphtheritic paralysis consists of a degeneration in the particular peripheral nerve supplying the paralyzed part and, in long standing cases, a marked degree of change in the muscles themselves.

Pott's Paralysis. In from 5 to 6 per cent of all cases of Pott's disease paralysis may occur. The usual site is the upper and middle dorsal region, where the canal is smallest and the fixation least efficient. The paralysis results from the compression of the cord with interference to the blood and lymphatic circulation, increase in the connective tissue and degeneration of the nervous elements. The compression may be due occasionally to displacement of bone, but usually to the breaking through into the canal of the tuberculous process in the bodies of the vertebrae with pressure on the cord by inflammatory products and thickening of the cord coverings. Actual destruction of the cord by tuberculous disease is rare, and even much compression may be recovered from. Pressure on

the spinal nerves before, or just after their exit may be the cause of this form of paralysis irrespective of injury to the cord proper.

Infantile Spinal Paralysis, or poliomyelities, is by far the most important of the causes of paralysis in early life. At the Hospital for the Ruptured and Crippled, in a series of 2,028 cases of nervous trouble, 75 per cent were poliomyelitis, 20 per cent were due to cerebral disease, and the remaining 5 per cent covered all other types of cases. In another series of 611 cases, 463 were poliomyelitis, 121 paralysis of cerebral origin, 16 were cases of obstetrical paralysis, 4 were cases of pseudohypertrophy, and 7 were miscellaneous cases.

Poliomyelitis occurs sporadically and epidemically. It occurs oftenest in summer, the months from June to September showing over 70 per cent of the cases. In some epidemics, dry weather and low water seemed factors. Children in the first three years of life present 77 per cent of the cases. Both sexes are affected equally and the strong as well as the weak.

The disease seems to be an infection dependent upon the action of a specific micro-organism, which, however, has not yet been satisfactorily determined, though a diplococcus was isolated in several of the cases of the Norway epidemic of 1903-1905, cultures of which, injected into mice, rabbits and dogs, uniformly produced paralysis of the hind legs. Many observers, however, have failed to find any organisms in spinal fluid or cord. Others have reported lesions of the cord similar to those of poliomyelitis in lead and arsenic poisoning.

The communicability of the disease is evident from the occurrence of epidemics and by the number of authenticated instances of several cases in the same family, and of the development of the disease soon after exposure. The digestive tract may be the portal of entry. Pointing to this are the occurrence of the disease in summer and the frequence of gastrointestinal disturbance at the outset. Milk may be the carrying agent, and a toxin liberated in the intestines by some anaerobic bacterium, carried to the spinal cells by the blood current, may be the actual cause of the changes in the cord.

Examination of the cerebrospinal fluid shows it to be almost uniformly clear and colorless, usually without cellular elements, or with only a few mononuclear leukocytes. On culture, unless con-

taminated, it usually has been found sterile by most competent observers.

The anatomical lesions are confined to the central nervous system, occurring most markedly in the enlargement of the spinal cord. In cases dying early in the disease, microscopical examination shows a diffuse inflammatory process closely related to the blood vessels. This process is found chiefly in the gray matter of the anterior horns; it is noticeable, however, in the white matter and in the pia. This inflammation extends throughout the whole length of the cord, but is most pronounced in the cervical and lumbar enlargements. There is an infiltration of small and large mononuclear leukocytes in the white matter and in the pia, and of polymorphonuclear leukocytes in the gray matter. There is a marked degeneration of the ganglion cells over large areas of the cord, and the inflammation is of wider extent than the clinical symptoms would indicate. Hemorrhages are seen, and even hemorrhagic cavities, in the anterior horns. The lesions in the pia are found to correspond to the degenerations in the anterior horns, but to be of greater extent than the inflammation in the gray matter. It seems evident from this that the infection occurs first in the spinal fluid and the pia, and extends along the blood vessels to the ganglion cells. In fact, the pia over the medulla pons, cerebellum and cerebrum is often found to be the site of inflammation when there is microscopically no evidence of inflammation in the gray matter there and when clinically the cases show merely paralysis of the extremities. In the severest cases with a picture of poliomyelitis and encephalitis, degeneration is found in the gray matter everywhere. The wide extent of the inflammation in all cases, however slight the clinical manifestations may be, and the occurrence of cases with bulbar and cerebral symptoms with a pathology similar to the mild cases, bring into our present idea of infantile spinal paralysis the clinical types of Landry's paralysis and encephalitis.

The lesions found in cases dying some time after the onset of the disease are sclerosis of the affected areas in the cord, degeneration of their peripheral nerves and atrophy of the muscles.

Infantile Cerebral Paralysis is second only to infantile spinal paralysis in the frequency of its occurrence, as the figures from the Hospital for the Ruptured and Crippled, already quoted, show.

Paralyses of this type may be congenital or acquired, the former being the more frequent. The congenital cases usually show paralysis during the first year. They may be due to causes within the uterus or to injury during labor. In the former cases there may be a history of neurotic taint in the family of the nature of hereditary epilepsy or insanity; there may be an accident or an injury during the later months of gestation, or wasting illness on the part of the mother. Syphilis is a doubtful cause. The anatomical lesions here are of the nature of large defects—half or more of one hemisphere, or of both, may be wanting or some parts may be poorly developed. The condition of agenesis corticalis, in which there is a defective development in the pyramidal cells in all parts of the brain, may be present. Defects in the development of the pyramidal tract may be a cause.

The congenital cases occurring at birth are due to meningeal hemorrhage and secondary changes—chronic meningoencephalitis, sclerosis or the formation of cysts. The most frequent cause of such a hemorrhage is tedious labor. Less often the hemorrhage is due to the pressure of forceps during delivery, while it may be a part of the hemorrhagic disease of the newly born, of syphilis, or of an infection. To the great extent of the lesions in the antenatal cases, and because in the birth palsies both hemispheres are exposed to the effect of the trauma, is due to the fact that congenital cases have characteristically diplegias and paraplegias as contrasted with the hemiplegias of the acquired form.

The cases of acquired cerebral paralysis are usually seen before the fifth year and, as stated, are characteristically hemiplegias. The paralysis may follow traumatism; it may occur in the course of infectious diseases such as scarlatina, measles, diphtheria, small-pox, pneumonia or whooping-cough. In whooping-cough the mechanical force of the paroxysms probably has considerable effect. A cerebrospinal meningitis from which the child recovers may set up a chronic meningitis which will result in paralysis. Convulsions are regarded both as the cause of paralysis and as an evidence of its beginning. They are probably causative factors.

The primary lesions found in these cases are hemorrhage, usually meningeal, embolism, thrombosis, chronic meningitis and encephalitis.

The secondary lesions are the usual sclerosis and atrophy, with degeneration of the pyramidal tract.

In conclusion, I would merely repeat that paralysis in early life may be due to lesions in any part of the motor tract; that they may be caused by any one of several factors; that a number of clinical affections which cause paralysis exist, but that poliomyelitis and cerebral lesions cause an overwhelming majority of the cases.

SMALLPOX VACCINATION WITH SUBSEQUENT OCCURRENCE OF POLIOMYELITIS. R. Siegert. (Schweiz. med. Wchnschr., 85:329-331, April 2, 1955). Three hundred thirty children, including all 12-year-olds, were revaccinated against smallpox in a small town in Western Germany on May 19 and 21, 1952. The same vaccine that had been prepared in a state vaccination institute was used in all the revaccinated children, four of whom became ill with severe poliomyelitis, two on the 31st, one on the 33rd and one on the 54th day after the revaccination. On the eighth day after the revaccination a "nodular reaction" to the vaccine had been observed in the upper arm of these children. The course of the vaccination was entirely normal. The vaccination was performed shortly before the onset of a poliomyelitis epidemic. Vaccination did not result in a more than fortuitously increased incidence of poliomyelitis among the vaccinated children, nor did vaccination cause any change in the course of the disease, since, in three of the four children, the vaccinated left arm was not affected by paralysis, and in the fourth child the paraylsis of the vaccinated arm was much less severe than that in the other arm. According to present-day knowledge a relationship between poliomyelitis and vaccination may be considered only when the vaccinated extremity alone or in combination with other areas of the body is affected by paralysis within 30 days after the vaccination. The time of onset of the poliomyelitis in the author's four patients makes it very likely that the infection occurred only when the phase of altered susceptibility, that might have been the result of revaccination, had already past. A relationship between poliomyelitis and preceding revaccination against smallpox, therefore, must be rejected in the author's patients. —*J. A. M. A.*

DEPARTMENT OF ABSTRACTS

MONEY, J., HAMPSON, J. G. AND HAMPSON, J. L.: HERMAPHRODITISM: RECOMMENDATIONS CONCERNING ASSIGNMENT OF SEX, CHANGE OF SEX AND PSYCHOLOGIC MANAGEMENT. (Bulletin Johns Hopkins Hospital, 97:284, Oct. 1955).

There are seven sexual variables which may operate independently of one another in hermaphroditism. They are: chromosomal sex; gonadal sex; hormonal sex; external genital morphology; accessory internal genital morphology; assigned sex and rearing; and gender role, including psychosexual orientation, which becomes built-up through experiences encountered and transacted. On the basis of chromosomal, gonadal and hormonal sex, seven varieties of hermaphroditism have been described, but these three criteria, singly or together, are never sufficient when practical decisions about assignment or change of sex have to be made. In the case of neonatal and very young infant hermaphrodites, we recommend that sex be assigned primarily, though not exclusively, on the basis of the external genitals and how well they lend themselves to surgical reconstruction in conformity with assigned sex due allowance being made for a program of hormonal intervention, if indicated. For older hermaphroditic infants, children and adults, we recommend that first consideration be given to the degree that a gender role has been indelibly established in the sex already assigned, and that changes of sex be scrupulously avoided, except in rare and carefully appraised instances, in order to avoid hazardous psychiatric sequelae. Judged in conjunction with each of the seven clinically recognizable varieties of hermaphroditism, these recommendations make eminent practical sense. A case is reported to illustrate the methods of studying attitudes and diagnosing gender role and applying these concepts in practical decisions. The psychologic management of parents of hermaphrodites and of patients themselves, with special reference to genital surgery, derives in its specific details from a general policy of frank and straightforward discussion and explanation. A clear and explicit understanding of basic principles is a prerequisite to frank and straightforward discussion. AUTHORS' SUMMARY.

CRAIG, J. O.: ORAL FACTORS IN ACCIDENTAL POISONING. (Archives Disease in Childhood, 30:419, Oct. 1955).

The case histories of 25 poisoned children are reviewed, and it is found that there is a much higher incidence of exaggerated oral traits, often amounting to pica, in this group than in a control series. It is stressed that this is no reason for relaxing the customary precautions against accidental poisoning in childhood. The theory is put forward that there are two main groups of poisoned children. There is a large group, showing exaggerated oral traits, and a smaller group showing no such abnormality. The individual risk of death is probably greater in the former than in the latter group. AUTHOR'S SUMMARY.

BODIAN, D., FRANCIS, T. JR., LARSON, C., SALK, J. E., SHOPE, R. E., SMADEL, J. E., AND SHANNON, J. A.: INTERIM REPORT, PUBLIC HEALTH SERVICE TECHNICAL COMMITTEE ON POLIOMYELITIS VACCINE. (Journal American Medical Association, 159:1444, Dec. 10, 1955).

The Technical Committee on Poliomyelitis Vaccine is of the opinion that the principle factors that were involved in earlier manufacturing and testing difficulties have been identified and corrective measures have been taken. Among these factors is the absolute need for removal of particles within which virus may be protected from inactivation by formaldehyde. Provisions have been made to insure as far as possible the removal of such protected particles by suitably spaced filtration procedures. In addition, the safety-test program has been strengthened by improved sampling procedures in the tissue culture tests and by increasing the sensitivity of the monkey safety tests. These measures, together with continuous review of plant production records, assure the safety of released vaccine and should make possible an increased availability of vaccine. AUTHORS' SUMMARY.

LAWRENCE, R. AND CARMICHAEL, D. B.: MYOCARDITIS IN ACUTE POLIOMYELITIS. (United States Armed Forces Medical Journal, 6:1817, Dec. 1955).

Although the exact role of myocarditis per se as a fatal complication in poliomyelitis is difficult to determine, it is apparent that it

is a common complication. The clinical diagnosis of myocarditis may be exceedingly difficult because of severe systemic reaction coupled with neurologic involvement. The electrocardiogram may be of significant assistance in the clinical diagnosis. Two cases of acute myocarditis, associated with poliomyelitis, are presented. In the first patient, the neurologic findings predominated; in the second, cardiac abnormalities obscured the presence of poliomyelitis, which was still unsuspected at the time of the patient's death. Of 15 patients dying of bulbospinal poliomyelitis at this hospital during a 6-year-period, 14 demonstrated autopsy evidence of myocarditis. AUTHORS' SUMMARY.

ROBERTS, M. H. AND SULLIVAN, C.: INFLUENCE OF THE LIVER ON BONE METABOLISM. Report of Two Cases. (Journal American Medical Association, 159:1002, Nov. 5, 1955).

Of 2 cases of extensive osteoporosis accompanying fatal liver disease, in one instance the process of decalcification occurred in a child whose bone structure was normal at the beginning of the illness. While under observation for cirrhosis of the liver, the patient developed extensive osteoporosis. One year later the pathology in the liver became carcinomatous. In the second child, the pathology in the bones was evidently of long standing, resulting not only in decalcification but also in some fundamental change in bone matrix. Neither therapy nor the course of the disease appeared to change the basic skeletal pathology. The patient in case 1 presented a puzzling problem. Decalcification occurred during a period in which the so-called cirrhotic liver shrank from 13 cm. to 8 cm. below the costal margin, despite intensive therapy. Subsequently, complete healing of bone took place as the liver diminished in size to only 5 cm. below the costal margin. The final invasion of the liver by carcinomatous cells resulted in no recurrence of osteoporosis. Such a sequence of events suggests that infection and subsequent cirrhosis were of prime importance in producing decalcification and that malignancy per se was not to be considered as an etiologic factor. MICHAEL A. BRESCIA, M.D.

CLARK, D. E.: ASSOCIATION OF IRRADIATION WITH CANCER OF THE THYROID IN CHILDREN AND ADOLESCENTS. (Journal American Medical Association, 159:1007, Nov. 5, 1955).

In 15 cases of carcinoma of the thyroid in children 15 years of age and younger, all the patients had prior x-ray therapy in infancy and early childhood for benign conditions about the head, neck and thorax. The observation lends strong support to the idea that an association exists between irradiation and the subsequent development of cancer of the thyroid in late childhood and adolescence. The interval from the time of irradiation to the date of diagnosis of the carcinoma averaged 6.9 years. The statistics presented show that, during the period from 1900 to 1950, cancer of the thyroid in individuals under 15 years of age was being diagnosed with increasing frequency. This increasing incidence correlates with the increased use of x-ray in the treatment of enlarged thymus, enlarged tonsils and adenoids, cervical adenitis and benign pulmonary conditions. The correlation suggests that prior irradiation about the neck in early life might be an etiological factor in the development of carcinoma of the thyroid in late childhood and adolescence. MICHAEL A. BRESCIA, M.D.

HANDY, V. H. AND GOLDBERG, I. D.: THE OCCURRENCE OF MALIGNANCIES IN CHILDREN. (New York State Journal of Medicine, 56:258, Jan. 15, 1956).

The incidence of reported cases of malignancy in children under 15 years of age for the period 1942 through 1953 in New York State, exclusive of New York City, is presented. There is no evidence of any decline in the incidence of these malignancies. The age group most affected by these malignancies is the very young, namely, the zero to 4 year age group. By far the most frequently occurring form of malignancy in each of the age groups (0-4, 5-9, 10-14) is leukemia. It is hoped that as physicians become more aware of the frequency of malignant disease in early life, particularly in the very young, the diagnosis will be made sooner. This in turn will allow more opportunity for therapy and will enhance the possibility of improved survivorship.

AUTHORS' SUMMARY

BOOK REVIEWS

PSYCHOPATHOLOGY AND EDUCATION OF THE BRAIN-INJURED CHILD. By Alfred A. Strauss and Newell C. Kephart with the collaboration of Laura E. Lehtinen and Samuel Goldenberg. Cloth. Pp. 266. Illustrated. Price $6.00. New York: Grune & Stratton, Inc., 1955.

This is a second volume devoted as the authors choose for their sub-title, "Progress in Theory and Clinic." The first volume was devoted to the "Fundamentals and Treatment of Brain-Injured Children." The book is quite involved and difficult to read except possibly for the "afficionado" of the subject. The book traces the development of perception, concept formation, language and behavior and how these developments differ in the normal and brain-injured child. The volume is well put together, has an extensive bibliography and no doubt will be of interest to those who concern themselves with this particular subject.

MICHAEL A. BRESCIA, M.D.

COMMUNICABLE DISEASES. 3rd Edition. By Franklin H. Top, A.B., M.D., M.P.H., F.A.C.P., F.A.A.P., F.A.P.H.A. and Collaborators. Cloth. Pp. 1208. Illustrated. Price $18.50. St. Louis: C. V. Mosby Company, 1955.

This is an excellent text covering the communicable diseases. The opportunity to see some of these diseases is getting less and less but the knowledge of these diseases remains important. In that regard the book is important and could be improved by including many more pictures of the rashes both typical and atypical. There are several minor criticisms. Vaccination of the thigh in the female infant is condoned whereas it should be criticized because the chances of secondary infection in that location are greater and at the present time there is no cosmetic advantage of a scar on the thigh as contrasted to one on the arm. The picture on page 320 shows the opening of a steam tube dangerously close to the infant. No mention is made of roseola infantum as a separate entity and the name roseola was inadvertently used as a synonym for measles. I wonder if the practical usefulness of a text of this nature might be increased by placing the diseases in alphabetical order rather than by the mode of entry of the infecting organism.

MICHAEL A. BRESCIA, M.D.

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1. Grayzel, H. G., Heimer, C. B., and Grayzel, R. W.: New York St. J. Med. 53:2233, 1953. 2. Heimer, C. B., Grayzel, H. G., and Kramer, B.: Archives of Pediatrics 68:382, 1951. 3. Behrman, H. T., Combes, F. C., Bobroff, A., and Leviticus, R.: Ind. Med. & Surgery 18:512, 1949. 4. Turell, R.: New York St. J. Med. 50:2282, 1950. 5. Marks, M. M.: Missouri Med. 52:187, 1955.

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